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GB04/50040



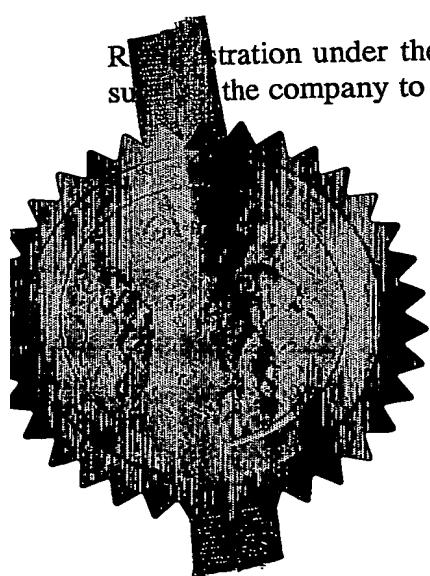
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Stephen Hardley

Dated 11 January 2005

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 P01/7700 0.00-0328650.7 ACCOUNT CHA

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office
 Cardiff Road
 Newport
 Gwent NP9 1RH

1. Your reference **GBP290096**

0328650.7

11 DEC 2003

2. Patent application number
 (The Patent Office will fill in this part)

3. Full name, address and postcode of the or of
 each applicant (underline all surnames)

AIMSCO Limited,
 4 Gildredge Road
 Eastbourne
 East Sussex BN21 4RL
 United Kingdom

8619546001

Patents ADP number (if you know it)

If the applicant is a corporate body, give the
 country/state of its incorporation

United Kingdom

4. Title of the invention **Treatment of Equines**

5. Name of your agent (if you have one)

"Address for service" in the United Kingdom
 to which all correspondence should be sent
 (including the postcode)

Marks & Clerk
 66-68 Hills Road
 Cambridge
 CB2 1LA

Patents ADP number (if you know it) **721125003** **Y8001**

6. Priority: Complete this section if you are declaring priority from one or more earlier patent applications, filed in the last 12 months	Country	Priority application No (if you know it)	Date of filing (day / month / year)
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7. Divisionals, etc: Complete this section only if this application is a divisional, application or resulted from an entitlement dispute	Number of earlier application	Date of filing (day / month / year)
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8. Is a Patents Form 7/77 (Statement of inventorship and of right to grant of a patent) required in support of this request?	Yes
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(Answer 'Yes' if:

- a) any applicant named in part 3 is not an inventor, or
- b) there is an inventor who is not named as an applicant, or
- c) any named applicant is a corporate body.

See note (d))

Patents Form 1/77

1. Accompanying documents: A patent application must include a description of the invention. Not counting duplicates, please enter the number of pages of each item accompanying this form:

Continuation sheets of this form	0
Description	5
Claim(s)	<i>D</i>
Abstract	
Drawing(s)	

10. If you are also filing any of the following, state how many against each item.

Priority documents
Translations of priority documents
Statement of Inventorship and right to grant of a patent (Patents Form 7/77)
Request for preliminary examination and search (Patents Form 9/77)
Request for substantive examination (Patents Form 10/77)
Any other documents (please specify):

11. We request the grant of a patent on the basis of this application.

Signature(s) *Marks & Clerk* Date: 11 December 2003

12. Name and daytime telephone number of person to contact in the United Kingdom

Cambridge Office
01233 345520

M&C Folio: GBP290096

Treatment of equines

FIELD OF THE INVENTION

The present invention relates to a method of treatment of chronic pulmonary disease in animals; in particular, but not exclusively, the invention relates to a method of treatment of equine chronic obstructive pulmonary disease. Certain aspects of the invention relate to a medicament for treatment of such diseases.

BACKGROUND OF THE INVENTION

Equine chronic obstructive pulmonary disease (COPD), also known as heaves or broken wind, is a respiratory disorder of horses. COPD is caused by inflammation of airways in response to particular allergens, and may result in difficult breathing, nasal discharge, exercise intolerance, and anxiety in the affected animal. In certain cases, secondary bacterial infections may also occur.

Incidence of COPD in horses in parts of northern Europe is believed to be as high as 50%, while a lower, but still common, incidence rate is reported from the northern United States. Besides being frequent, equine COPD may eventually lead to decreased performance capacity, to early retirement from sporting activity, and ultimately to euthanasia.

Typical allergens responsible for COPD include dust, moulds, hay, straw, pollens, and the like. The preferred treatment for COPD is to isolate the affected animal from the allergens; however, it will be appreciated that this may not always be possible. An alternative, or additional, treatment may be administration of anti-inflammatory agents to reduce the severity of attacks. Conventional anti-inflammatory agents include antihistamines, steroids, and bronchodilators.

There is a need for an alternative treatment for COPD.

PCT publications WO 03/004049 and WO 03/064472 describe therapeutic agents and treatments which are based on a serum composition with many surprising beneficial effects. The respective content of each of these two texts is incorporated in full by specific reference. In particular, the reader is referred to them for an understanding of how the therapeutic agent can be prepared, and for the indications which can be treated.

Typically a goat is immunised with HIV-3B viral lysate raised in H9 cells. The resulting serum is believed to be active against HIV, and multiple sclerosis. The reader is further referred in particular to the section on pages 3 and 4 of WO03/004049 headed 'Example of Production of Goat Serum' for further details of the production of serum. This section is incorporated herein by reference.

In addition to the uses described in the earlier PCT publications, it has been surprisingly identified that the serum composition may be active against equine COPD.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention, there is provided a method of treatment of a pulmonary inflammatory disorder in an equine, the method comprising administering a serum composition obtained from a goat after challenge with an immunogen.

The immunogen may comprise HIV. This may be presented in intact host cells, in cell-free extracts, as a viral lysate, or in a mixture thereof.

Alternatively, in a variation of the invention, following heat inactivation of a supernate solution upon which a viral culture has been grown or which is capable of the same, but has not been used to grow a culture, may also be used as an immunogen which will produce a suitable response. Any supernate solution or other medium which is suitable for the in vitro growth of HIV or another virus may be used to produce an acceptable immunogen, which will produce an effective response. The supernate of a cell culture growth medium such as PMBC or the cancer immortal cell line as used to grow HIV 3b are given as an example. The HIV or other selected virus does not need to be present to produce an effective immunogen to create the composition.

Other suitable immunogens are recited on pages 12 and 13 of WO03/064472, the contents of which are incorporated herein by reference.

The animal to be treated is preferably a horse.

The pulmonary inflammatory disorder to be treated is preferably a chronic disorder, and more preferably chronic obstructive pulmonary disease.

An example of preparation of goat serum is given below.

The serum composition is preferably administered in a dosage of between 1 and 20 mg of composition to the equine; more preferably between 4 and 15 mg, and most preferably between 6 and 10 mg. The precise dosage to be administered may be varied depending on such factors as the age, sex, and weight of animal, the method and formulation of administration, as well as the nature and the severity of the disorder to be treated. Other factors such as diet, time of administration, condition of the animal, drug combinations, and reaction sensitivity may be taken into account.

The serum composition may be administered by any effective route, preferably by subcutaneous or intramuscular injection, although alternative routes which may be used include oral, aerosol, parenteral, or topical.

An effective treatment regimen may be determined by the clinician or veterinarian responsible for the treatment, and may depend on factors such as the age, sex, weight of the animal, the method of administration, and the nature and severity of the disorder to be treated. Other factors such as diet, time of administration, condition of the animal, drug combinations, and reaction sensitivity may be taken into account. One preferred regimen for the treatment of equine COPD is the intramuscular injection of between 6 and 15 mg of serum composition in a liquid formulation once daily for one week.

The serum composition may, but need not, comprise anti-HLA antibody. It is believed that this may play a role in the activity of the serum.

A further aspect of the invention provides a method of treatment of a pulmonary inflammatory disorder in an equine, the method comprising administering a serum composition obtainable from a goat after challenge with an immunogen.

The present invention also provides the use of a serum composition obtained from a goat after challenge with an immunogen in the manufacture of a medicament for the treatment of a pulmonary inflammatory disorder in an equine. The use of a serum composition obtainable from a goat after challenge with an immunogen in the

manufacture of a medicament for the treatment of a pulmonary inflammatory disorder in an equine is also provided.

Also provided is a pharmaceutical composition for the treatment of a pulmonary inflammatory disorder in an equine, the composition comprising a serum composition obtained from a goat after challenge with an immunogen, suitable for administration to a subject animal.

Examples of pharmaceutical compositions include any solid (tablets, pills, capsules, granules, etc) with suitable composition for oral, topical, or parenteral administration; fluids suitable for injection; or aerosols suitable for administration to an animal. The compositions may include a carrier.

According to a further aspect of the present invention, there is provided a method of treatment of a pulmonary inflammatory disorder in an equine, the method comprising administering a serum composition comprising anti-HLA antibody. It is believed that at least a component of the serum activity is linked with anti-HLA activity; the activity may reside in the antibody itself or in some other factor associated with the antibody. Preferably the anti-HLA antibody is goat anti-HLA antibody. The antibody may be polyclonal.

DETAILED DESCRIPTION OF THE INVENTION

Example of Production of Goat Serum

A goat was inoculated by intramuscular injection with lysed HIV viral cocktail and formulated with Freunds adjuvant. The virus was previously heat killed at 60°C for 30 minutes. Blood samples were drawn after an appropriate interval, such as two weeks, for initial assessment. In the optimised procedure, the goat is injected every week for four weeks, then at six weeks the animal is bled to obtain the reagent.

Approximately 400 cc of blood is drawn from the goat under sterile technique. The area for needle extraction is shaved and prepared with betadine. An 18-gage needle is used to draw approximately 400 cc of blood from the animal. Of note is that the animal can tolerate approximately 400 cc of blood drawn without the animal suffering

any untoward effects. The animal does not have to be sacrificed. The animal can then be re-bled in approximately 10 to 14 days after it replenishes its blood volume.

The presence of potentially useful antibodies was confirmed, having regard to the desired antibody activity. Once the presence of such reagents was confirmed, blood was then taken from the goat at between 4-6 weeks.

The base blood product in order to create the reagent is then centrifuged to create the serum. 300 ml of serum was then filtered to remove large clots and particulate matter. The serum was then treated with supersaturated ammonium sulphate (45% solution to room temperature), to precipitate antibodies and other material. The resulting solution was centrifuged at 5000 rpm for five minutes, after which the supernatant fluid was removed. The precipitated immunoglobulin was resuspended in phosphate-buffered saline (PBS buffer, see Sambrook et al, 'Molecular Cloning: A Laboratory Manual', 1989) sufficient to redissolve the precipitate.

The solution was then dialysed through a membrane with a molecular weight cut off of 10,000 Daltons. Dialysis was carried out in PBS buffer, changed every four hours over a period of 24 hours. Dialysis was carried out at 4°C.

After 24 hours of dialysis the contents of the dialysis bag were emptied into a sterile beaker. The solution was adjusted such that the mass per unit volume = 10 mg per ml. The dilution was carried out using PBS. The resulting solution was then filtered through a 0.2 micron filter into a sterile container. After filtration, the solution was aliquoted into single dosages of 1ml and stored at -22°C prior to use.

Administration of serum

A 1 ml aliquot of serum, prepared as described, is injected intramuscularly to a horse suffering from COPD. The treatment is repeated daily for seven days.

Document made available under the Patent Cooperation Treaty (PCT)

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